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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR   | ATTORNEY DOCKET NO.     | CONFIRMATION NO.       |
|---|-------------|------------------------|-------------------------|------------------------|
| 10/553,669  | 08/09/2006  | Stephen M Strittmatter | 2159.0470001/EJH/SAC    | 4039                   |
| 53644 7590 12/11/2007<br>STERNE, KESSLER, GOLDSTEIN & FOX, P.L.L.C.<br>1100 NEW YORK AVE., N.W.<br>WASHINGTON, DC 20005 |             |                        | EXAMINER<br>HA, JULIE   |                        |
|   |             |                        | ART UNIT<br>1654        | PAPER NUMBER           |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |  |  |
|------------------------------|--------------------------------------|--|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/553,669 | <b>Applicant(s)</b><br>STRITTMATTER ET AL. |  |
|                              | <b>Examiner</b><br>Julie Ha          | <b>Art Unit</b><br>1654                    |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 10 October 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 42-61 is/are pending in the application.
- 4a) Of the above claim(s) 48, 50, 57, 59 and 61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 42-47, 49, 51-56, 58 and 60 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Amendment after Non-final rejection filed on October 10, 2007 is acknowledged. Claims 42-61 are pending in this application. Applicant elected species SEQ ID NO:3 with traverse in the reply filed on June 08, 2007. The Restriction requirement was deemed proper and made FINAL in the previous office action. Claims 48, 50, 57, 59 and 61 remain withdrawn from further consideration as being drawn to nonelected species. Claims 42-47, 49, 51-56, 58 and 60 are examined on the merits in this office action.

### ***Withdrawn Objections***

1. Objection to the title is hereby withdrawn due to Applicant's arguments and amendment changing the title to "Nogo Receptor-1 Polypeptides for the Treatment of Conditions Involving Amyloid Plaques."
2. Objection to the specification is hereby withdrawn due telephone interview conducted on September 17, 2007 and in review of the specification filed on October 17, 2007. The specification as filed do not have the spelling or grammatical errors at paragraph [0016], line 5 and paragraph [0069], line 22.

### ***Withdrawn Rejections***

3. Rejection under 35 U.S.C. 112, 2nd paragraph is hereby withdrawn due to Applicant's amendment to the claim.
4. Rejection under 35 U.S.C. 112, 1st paragraph under enablement is hereby withdrawn due to Applicant's amendment to the claims and arguments.

5. Rejection under 35 U.S.C. 102(b) is hereby withdrawn due to Applicant's arguments and amendments to the claims.

***Maintained Rejections***

***35 U.S.C. 112, 1<sup>st</sup>***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 42-47, 49, 51-56, 58 and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

8. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties,

functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP 2163.

9. Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

“A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

10. The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of

representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

11. In the instant case, the claims are drawn to a method for reducing the levels of A $\beta$  peptide in a mammal comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide. The generic statement a soluble Nogo receptor-1 polypeptide does not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

12. As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 42 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that make up the class of Nogo receptor-1 polypeptide. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples

in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules and other synthetic peptide or peptide-like molecule that can function as Nogo receptor-1 polypeptide.

13. The specification is limited to the peptide or peptide-like molecules that belong to the same class of protein, Nogo receptor-1 polypeptide. The specification disclosed that "Nogo receptor antagonist" means a molecule that inhibits the binding of Nogo receptor-1 to a ligand (e.g., NogoA, NogoB, NogoC, MAG, OM-gp) (see paragraph [0026]).

Further, the specification discloses that Nogo receptor antagonist may include soluble Nogo receptor-1 polypeptides, antibodies that bind to the Nogo receptor protein and antigen-binding fragments of such antibodies, and small molecule antagonists (see paragraph [0030]). The working example describes the Nogo receptor-1 polypeptide (both human and rat, SEQ ID NOS: 3-6) (see paragraph [0031]). The specification further discloses that Nogo receptor antagonist that is an antibody or an antigen-binding fragment thereof that specifically binds an immunogenic Nogo receptor-1 polypeptide and inhibits the binding of Nogo receptor-1 to a ligand and these antibodies may be produced in vivo or in vitro, recombinant, engineered, humanized and/or chimeric (see paragraph [0034]). The working example only describes the treatment with sNgR310 (SEQ ID NO:3) fused with immunoglobulin moiety Fc (sNgR310-Fc) to examine the role of NgR/APP/A $\beta$  interaction (see Example 6, paragraph [0069]). The specification does

not describe any other Nogo receptor-1 polypeptide, such as any other proteins or any other type of peptide or peptide-like molecule that act as Nogo receptor-1 polypeptide (such as small organic molecules). Descriptions of SEQ ID NOS: 3-6 and antibodies for Nogo receptor-1 polypeptide are not sufficient to encompass numerous other proteins and small molecules that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. As described above, GenBank Accession # Q86UN2, is a Nogo-66 receptor homolog (also reticulon-4 receptor-like 1 precursor). GenBank Accession Number NP 075358 is a reticulon-4 receptor from the mouse species. This comprises of 473 amino acids in lengths and comprises the same amino acid sequence of SEQ ID NO:3, thus would function as a Nogo receptor-1 polypeptide. Further, the specification does not describe any analogs and homologs of Nogo receptor-1 polypeptide and a description of peptide with up to 10 conservative amino acid substitution for SEQ ID NOS: 3-6 is not enough to encompass the derivatives. This is because SEQ ID NOS: 3-6 have 284 amino acids, 318 amino acids, 283 amino acids, and 317 amino acids, respectively. There are innumerable possibilities that encompass these conservative amino acid substitutions. For example, since SEQ ID NO:3 has 284 amino acids, there are infinite number of possible Nogo-1 receptor polypeptide sequences, due to the 284 amino acid residues. All 284 amino acids can have conservative amino acid substitutions. Furthermore, there are several naturally occurring amino acids that can be conservatively substituted. For example, A, G, P, S and T are functionally similar amino acids; N, D, Q, and E are functionally similar amino acids; R, H and K are functionally

similar amino acid, etc. Furthermore, the amino acid substitution can occur anywhere within the 284 residues. Additionally, there are non-natural amino acids, such as D-isomers,  $\beta$ -amino acid,  $\gamma$ -amino acid, and  $\epsilon$ -amino acids as well as amino acid mimetics that can be substituted conservatively. Further, the specification does not describe what small molecule would function as a Nogo receptor-1 polypeptide. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

14. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

### ***Response to Applicant's Arguments***

15. Applicant argues that "the present specification provides sufficient written description to convey to one of ordinary skill that Applicants had possession of the claims". Furthermore, Applicant "points out that the test for written description requirement is whether one skilled in the art can reasonably conclude that the inventor

has possession of the claimed invention in the specification as filed". Applicant points the Examiner to specification at page 7, line 16 through page 9, line 9 and Table 2.

16. Applicant's arguments have been fully considered but have not been found persuasive because specification does not describe that the Applicant was in possession of claimed invention at the time of application. The specification at page 7 and Table 1 describes that the full-length Nogo receptor-1 polypeptide of human and rat. The specification describes the full length Nogo receptor-1 (see p. 7, lines 19-22), not the polypeptide. The specification describes that "soluble Nogo receptor polypeptides used in the methods of the invention comprise an NT domain, 8 LRRs and an LRRCT domain and lack a signal sequence and a functional GPI anchor... suitable polypeptides include, for example, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO: 5 and SEQ ID NO: 6 (Table 2). The specification further describes that "a fusion protein that includes a soluble Nogo receptor polypeptide may be used" (see p. 9, paragraph [0033]). Applicant further described that "additional polypeptides which may be used in the methods of the invention are described, for example, in International Patent Applications PCT/US02/32007 and PCT/US03/25004. PCT/US02/32007 discloses that NgR derived polypeptide contains 27-309 of SEQ ID NO:2 (see p. 5, lines 20-22). The reference further discloses that the proteins or polypeptide has the human amino acid sequence depicted in SEQ ID NO:2 or the murine amino acid sequence depicted in SEQ ID NO:4. The protein or polypeptide also refers to the peptides that have the amino acid sequence depicted in SEQ ID NO: 8, 10, 12, 14, 16, 18 and 20 (all 25 amino acid residues) (see p. 20, lines 6-12). However, as described above, there are innumerable

possibilities that encompass these conservative amino acid substitutions. For example, since SEQ ID NO:3 has 284 amino acids, there are infinite number of possible Nogo-1 receptor polypeptide sequences, due to the 284 amino acid residues. All 284 amino acids can have conservative amino acid substitutions. Furthermore, there are several naturally occurring amino acids that can be conservatively substituted. For example, A, G, P, S and T are functionally similar amino acids; N, D, Q, and E are functionally similar amino acids; R, H and K are functionally similar amino acid, etc. Furthermore, the amino acid substitution can occur anywhere within the 284 residues. Additionally, there are non-natural amino acids, such as D-isomers,  $\beta$ -amino acid,  $\gamma$ -amino acid, and  $\epsilon$ -amino acids as well as amino acid mimetics that can be substituted conservatively. Further, the specification does not describe what small molecule would function as a Nogo receptor-1 polypeptide. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed. Therefore, the rejection is maintained.

***Rejection-35 U.S.C. 102***

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States

only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 42, 47, 49 and 58 are rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al (US Patent # 7029874).

19. The instant claims are drawn to a method for reducing the levels of A $\beta$  peptide in a mammal comprising administering a therapeutically effective amount of a soluble Nogo receptor antagonist comprises of SEQ ID NO: 3.

20. Baker et al teach polypeptides and nucleic acid molecules encoding those polypeptide (see abstract). The reference teaches SEQ ID NO: 400 (see SEQ ID NO: 400 enclosed) that comprises the SEQ ID NO:3. Since SEQ ID NO: 400 comprises SEQ ID NO:3, it inherently has the polypeptide functionality and activity. This reads on claims 42, 49 and 58. The reference further teaches that neurotrimin as well as other members of the IgLON subfamily have been identified to have effect upon neural patterning, differentiation, maturation and growth. Thus, PRO337, the human neurotrimin homolog would be expected to have utility in disease which are characterized by neural disfunction...can be used to treat human neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's Chorea, Down's Syndrome, nerve deafness, and Meniere's disease (see column 212, lines 14-30). Further, the reference teaches that PRO polypeptides may also be employed as therapeutic agents (see column 191, lines 20-21) and the route of administration is for example injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration or by sustained release systems (see column 191, lines 53-57).

Furthermore, the reference teaches when in vivo administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1mg/kg/day to 10 mg/kg/day, depending upon the route of administration (see column 192, lines 3-8). This reads on the therapeutically effective amount of the antagonist limitation. The reference is silent as to the reducing the levels of A $\beta$  peptide in a mammal. However, since the prior art teaches that the polypeptides can be used to treat Alzheimer's disease, and the human neurotrimin homolog would be expected to have utility in disease which are characterized by neural disfunction (such as AD), it would inherently reduce the levels of A $\beta$  peptide once administered to the mammal. Therefore, the prior art reads on claims 42, 47, 49 and 58.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

21. Claims 42, 47, 49 and 58 are rejected under 35 U.S.C. 102(a) as being anticipated by Baker et al (US Patent # 7029874).
22. The instant claims are drawn to a method for reducing the levels of A $\beta$  peptide in a mammal comprising administering a therapeutically effective amount of a soluble Nogo receptor antagonist comprises of SEQ ID NO: 3.
23. Baker et al teach polypeptides and nucleic acid molecules encoding those polypeptide (see abstract). The reference teaches SEQ ID NO: 400 (see SEQ ID NO: 400 enclosed) that comprises the SEQ ID NO:3. Since SEQ ID NO: 400 comprises SEQ

ID NO:3, it inherently has the polypeptide functionality and activity. This reads on claims 42, 49 and 58. The reference further teaches that neurotrimin as well as other members of the IgLON subfamily have been identified to have effect upon neural patterning, differentiation, maturation and growth. Thus, PRO337, the human neurotrimin homolog would be expected to have utility in disease which are characterized by neural disfunction...can be used to treat human neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's Chorea, Down's Syndrome, nerve deafness, and Meniere's disease (see column 212, lines 14-30). Further, the reference teaches that PRO polypeptides may also be employed as therapeutic agents (see column 191, lines 20-21) and the route of administration is for example injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration or by sustained release systems (see column 191, lines 53-57). Furthermore, the reference teaches when in vivo administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1mg/kg/day to 10 mg/kg/day, depending upon the route of administration (see column 192, lines 3-8). This reads on the therapeutically effective amount of the antagonist limitation. The reference is silent as to the reducing the levels of A $\beta$  peptide in a mammal. However, since the prior art teaches that the polypeptides can be used to treat Alzheimer's disease, and the human neurotrimin homolog would be expected to have utility in disease which are characterized by neural disfunction (such as AD), it

would inherently reduce the levels of A $\beta$  peptide once administered to the mammal.

Therefore, the prior art reads on claims 42, 47, 49 and 58.

***Response to Applicant's Arguments***

24. Applicant argues that "claim 42 is drawn to a method for reducing the levels of A $\beta$  peptide in a mammal, comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide...Baker does not disclose a soluble Nogo receptor-1 polypeptide. Baker only discloses the full-length sequence of Nogo receptor-1, which includes a glycosylphosphatidylinositol (GPI) anchor. Therefore, the Nogo receptor-1 polypeptide disclosed in Baker is not a soluble polypeptide, as required by the present claims". Furthermore, Applicant argues that "Baker does not teach how to use a soluble Nogo receptor-1 polypeptide to reduce the levels of A $\beta$  peptide in a mammal".

25. Applicant's arguments have been fully considered but have not been found persuasive, because Baker et al teach polypeptide SEQ ID NO: 400 (neurotrimin) that comprises the SEQ ID NO:3, and PRO337, the human neurotrimin homolog can be used to treat human neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's disease, etc (see column 212, lines 14-30). Further, the reference teaches that PRO polypeptides may also be employed as therapeutic agents and the route of administration is for example injection or infusion (see column 191, lines 20-21 and 53-57). The reference teaches the in vivo administration of PRO polypeptide or agonist or antagonist thereof. Since the route of administration can be injection or infusion, the polypeptides must be solubilized (i.e.,

peptides are soluble). Therefore, the reference meets the "soluble" polypeptide limitation. The reference is silent as to the reducing the levels of A $\beta$  peptide in a mammal. However, as described above, since the prior art teaches that the polypeptides can be used to treat Alzheimer's disease (AD), and the human neurotrimin homolog would be expected to have utility in disease which are characterized by neural dysfunction (such as AD), it would inherently reduce the levels of A $\beta$  peptide once administered to the mammal. Therefore, the rejection is maintained.

***New Rejection***

***35 U.S.C. 102***

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

26. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Eisenbach-Schwartz et al (US 2002/0072493 A1).

27. The instant claims are drawn to a method for reducing the levels of A $\beta$  peptide in a mammalian brain comprising administering a therapeutically effective amount of a soluble Nogo receptor-1 polypeptide.

28. Eisenbach-Schwartz et al teach methods to promote nerve regeneration or to confer neuroprotection and inhibit neuronal degeneration by administering NS-specific peptide derived therefrom or an analog or derivative of said peptide (see abstract). The reference teaches the use of the compositions to ameliorate the effects of disease that result in a degenerative process that includes Alzheimer's disease (see paragraph

[0125] and claim 5). This reads on claims 2-3. The reference further teaches that natural or synthetic NS-specific antigens are preferred to include...neurotransmitter receptors, Nogo and Nogo receptor (NgR) (see paragraph [0100]). Furthermore, the reference teaches that examples of peptides are immunogenic peptides derived from the Nogo protein sequence and peptides derived from the Nogo receptor (NgR), such as the 15-mer peptides of the sequences: SGVPSNLPQRLAGRD (SEQ ID NO: 28) or TRSHCRLGQAGSGSS (SEQ ID NO: 29) (see paragraphs [0110]-[0112]). The reference further teaches pharmaceutical compositions useful in methods to promote nerve regeneration or to inhibit neuronal degeneration in the CNS or PNS, comprising therapeutically effective amount of at least one ingredient...a peptide derived from an NS-specific...an analog or derivative of said peptide (see paragraphs [0130]-[0136]). The instant specification discloses that Nogo receptor-1 is also variously referred to as "Nogo receptor",..."NgR" and "NgR-1" (see paragraph [0031]). Since the reference teaches peptides derived from the Nogo receptor, it would inherently be a Nogo receptor-1 polypeptide. The reference is silent as to "reducing the levels of A $\beta$  peptide in a mammalian brain". However, since the prior art teaches that the polypeptides can be used to ameliorate the effects of disease that result in degenerative process that include Alzheimer's disease (AD) and teaches pharmaceutical composition in pharmaceutically effective amount, the peptide derived from NgR would inherently reduce the levels of A $\beta$  peptide once administered to the mammal.

***Conclusion***

29. No claims are allowed.

30. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

31. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982.

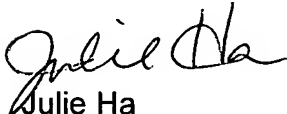
The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

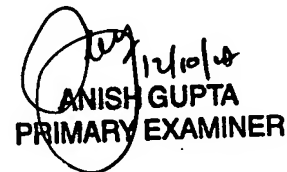
33. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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